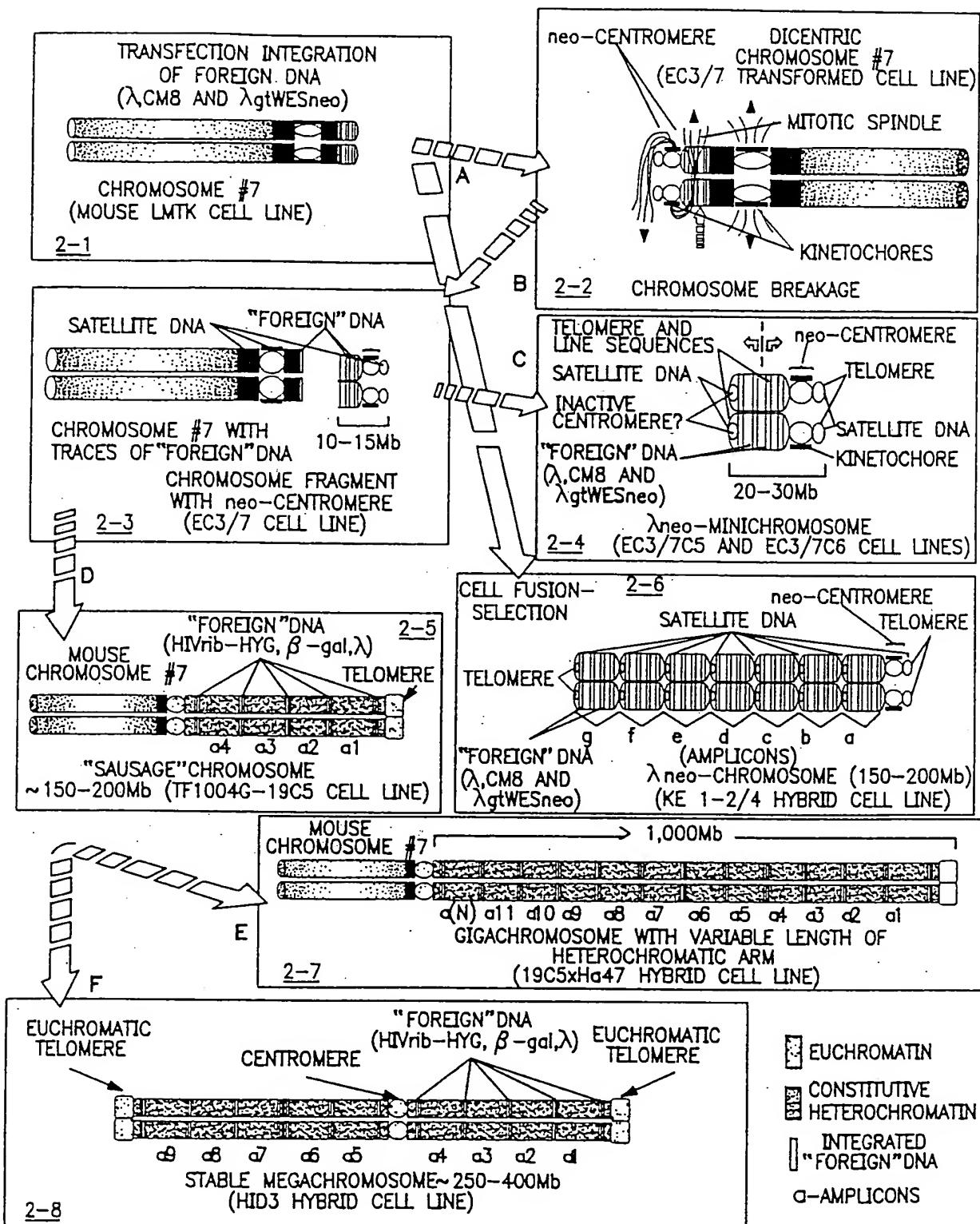
**FIG. I**

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ARTIFICIAL CHROMOSOMES, USES THEREOF AND
METHODS FOR PREPARING ARTIFICIAL CHROMOSOMES**FIG. 2**

FISH & RICHARDSON P.C.

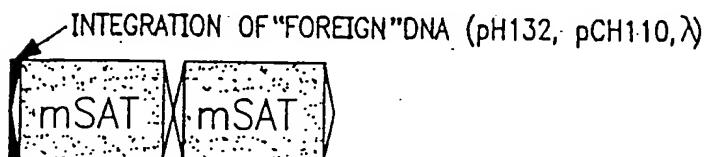
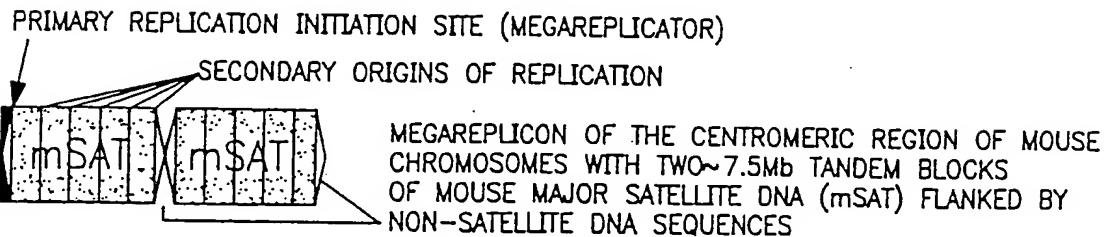
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ARTIFICIAL CHROMOSOMES, USES THEREOF AND
METHODS FOR PREPARING ARTIFICIAL CHROMOSOMES



REPLICATION ERROR GENERATES INVERTED MEGAREPLICONS



AMPLIFICATION PRODUCES A TANDEM ARRAY OF IDENTICAL CHROMOSOME SEGMENTS (AMPLICONS) THAT CONTAIN TWO INVERTED MEGAREPLICONS BORDERED BY THE HETEROLOGOUS ("FOREIGN") DNA

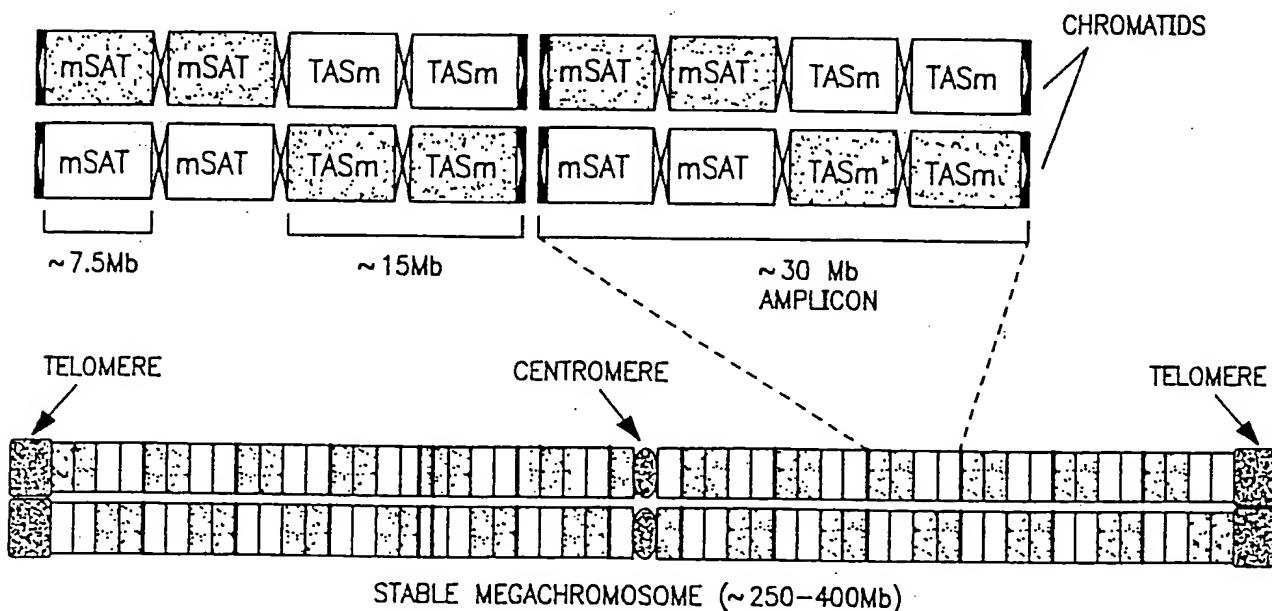


FIG. 3

EC3/7 MOUSE LMTK FIBROBLAST CELL LINE WITH neo-CENTROMERE
(HADLACZKY ET AL. PROC. NATL. ACAD. SCI. USA, 88:
8106-8110, 1991)

- DEPOSITED IN THE EUROPEAN COLLECTION OF ANIMAL CELL CULTURE (ECACC) ACCESSION NUMBER 9005 1001

↓ SINGLE-CELL SUBCLONING

EC3/7CS MOUSE LMTK FIBROBLAST CELL LINES WITH neo-MINICHROMOSOME
(HADLACZKY ET AL. PROC. NATL. ACAD. SCI. USA, 88:
8106-8110, 1991)

- COTRANSFECTION WITH PLASMIDS pH132 (HIVRIBOZYME,
HYGROMYCIN RESISTANCE) pCH110 (β -GALACTOSIDASE), AND
LAMBDA PHAGE (λ C1 875 SAM7) DNA, SELECTION
WITH HYGROMYCIN B.

TF1004G-19C5* - MOUSE LMTK FIBROBLAST CELL LINES WITH
neo-MINICHROMOSOME, AND STABLE "SAUSAGE" CHROMOSOME

-
- FUSION WITH CHINESE HAMSTER (CHO K20) CELL LINE,
↓ SELECTION WITH HYGROMYCIN B AND HAT.

19C5xHa4 - MOUSE-HAMSTER HYBRID CELL LINE CARRYING THE
neo-MINICHROMOSOME AND THE "SAUSAGE" CHROMOSOME,
 CONTAINING COMPLETE HAMSTER GENOME AND PARTIAL MOUSE
 GENOME.

↓ BrdU TREATMENT, SINGLE CELL CLONING, SELECTION:
G418 (NEOMYCIN) OR HYGROMYCIN, OR BOTH

G3DS* - MOUSE-HAMSTER HYBRID CELL LINE CARRYING THE
neo-MINICHROMOSOME AND THE MEGACHROMOSOME,
 CONTAINING COMPLETE HAMSTER GENOME AND PARTIAL
 MOUSE GENOME.

↓ H1D3* - MOUSE-HAMSTER HYBRID CELL LINE CARRYING
NO neo-MINICHROMOSOME BUT THE MEGACHROMOSOME, IS
 PRESENT, CONTAINING COMPLETE HAMSTER GENOME AND PARTIAL
 MOUSE GENOME.
↓ FUSION WITH CD4+ HeLa CELL LINE CARRYING THE
CD4 AND NEOMYCIN RESISTANCE GENE PLASMID CONSTRUCT
(CD4neo), SELECTION WITH G418 AND HYGROMYCIN B

H1xHe41* - MOUSE-HAMSTER-HUMAN HYBRID CELL LINE CARRYING THE
 MEGACHROMOSOME PRESENT, CONTAINING COMPLETE HAMSTER
 GENOME, AND PARTIAL MOUSE GENOME, AND A SINGLE HUMAN
 CHROMOSOME WITH INTEGRATED CD4neo CONSTRUCT (UNPUBLISHED).

↓ REPEATED BrdU TREATMENT, SINGLE-CELL CLONING

1B3 - SAME AS H1xHe41, BUT APPROXIMATELY 25% OF THE CELLS
ARE CARRYING A TRUNCATED MEGACHROMOSOME

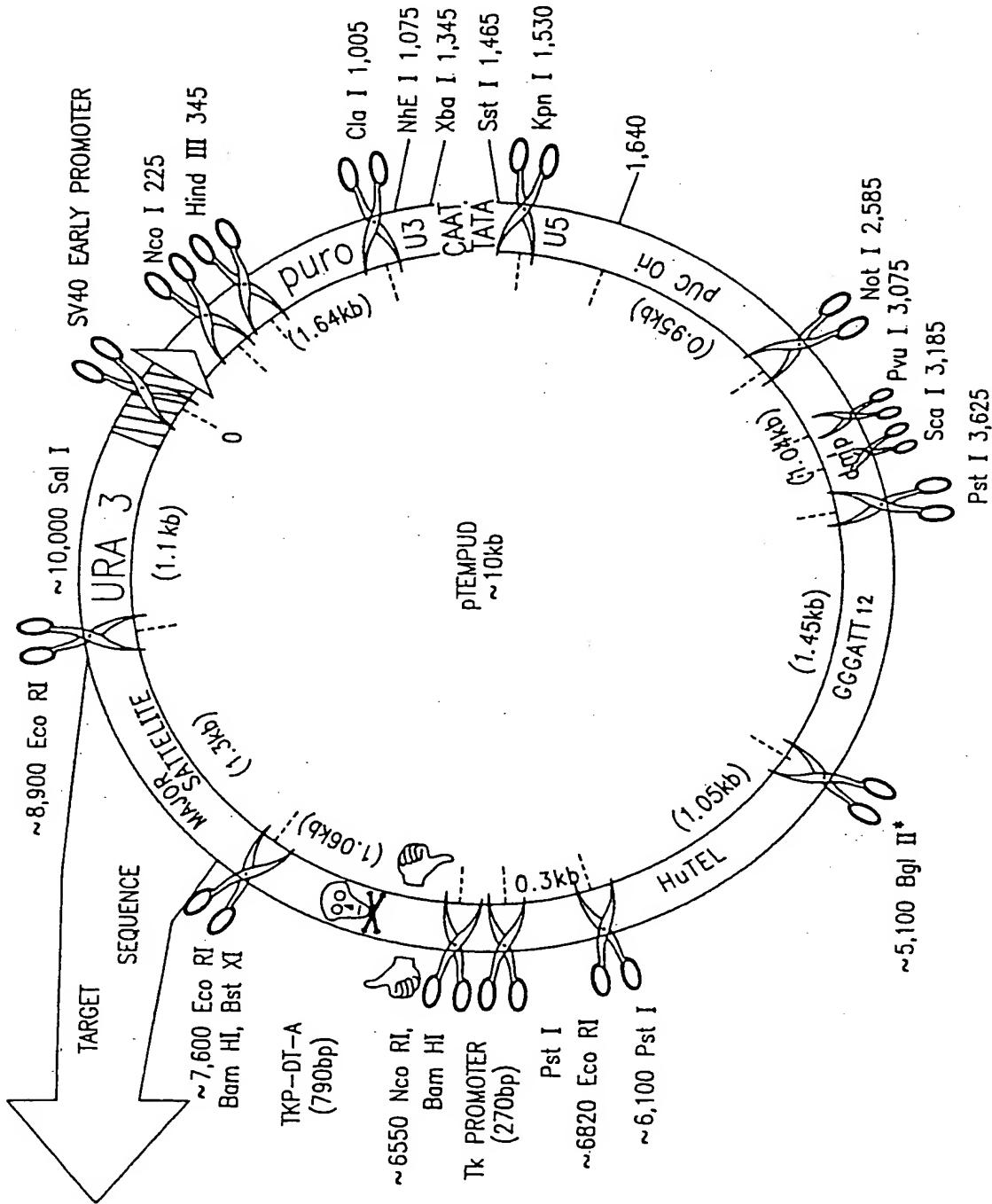


FIG. 5